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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/623,035	10/12/00	DURRANT	L 0380-P02284U

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EXAMINER	
DAVIS,N	
ART UNIT	PAPER NUMBER
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DATE MAILED:
10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/623,035	Applicant(s) DURRANT ET AL.	
	Examiner Natalie A. Davis	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,16,17,19 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,16,17,19 and 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

a. Group I, claim(s) 1-12, 16-17, 19, and 27-32, drawn to a cancer vaccine comprising a polypeptide of the CD55 family and a method of treating a patient with cancer.

b. Group II, claim(s) 13-15, drawn to a cancer vaccine comprising a nucleic acid of the CD55 family.

c. Group III, claim(s) 20-24, drawn to an isolated 791Tgp72 antigen and composition.

d. Group IV, claim(s) 26, drawn to a method of isolating 791Tgp72 antigen from cells.

2. The inventions listed as Groups I -IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions have been found by the examiner to have no special technical feature that defined a contribution over the prior art because the use of 791Tgp72 in a vaccine has already been described (Durrant, 1997) for use in the treatment of cancer. Since the inventions do not contribute a special technical feature when viewed over the prior art, they do not have a single inventive concept and lack unity of invention.

protein

The invention of Group I is drawn to a cancer vaccine comprising a nucleic acid of the CD55 family. The invention of Group II is drawn to a cancer vaccine comprising a nucleic acid of the CD55 family. The invention of Group III is drawn to an isolated 791Tgp72 antigen and composition. The invention of Group IV is drawn to a method of isolating 791Tgp72 antigen from cells.

3. The inventions are distinct, each from the other because of the following reasons: Inventions I-III (products) and IV (method) are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products of Groups I-III may be used to prevent the recurrence of cancer. The method of Group IV may be practiced using various therapeutic agents and do not necessarily have to be used with the products of Groups I-III. Materially different products, such as chemotherapy, may be used in the method of Group IV.

4. The products of Groups I,-III are structurally and functionally different, are drawn to structurally and functionally different molecules, each invention requires different reagents and steps to make and characterize them, or different methods of use that do not share common steps or reagents and rely on different endpoints.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, divergent subject matter, and require different search strategies, restriction for examination purposes as indicated is proper.

6. Applicant is advised that the response to this requirement, to be complete, must include an election of the invention to be examined even though the requirement be traversed.

7. During a conversation with Attorney Hagman on 25 July 2001 an election to the restriction requirement as indicated above was required. A voicemail message was received from Attorney Hagman on 2 August 2001, wherein a provisional election was made with traverse to prosecute the invention of Group I, claims 1-12, 16-17, 19, and 27-32. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-15, 20-24, and 26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-12, 16-17, 19, and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The elected claims are drawn to a cancer vaccine comprising a polypeptide of the CD55 family or a fragment or derivative thereof, wherein the vaccine is capable of inducing an immune response in a patient. The claims are further drawn to a vaccine wherein the polypeptide is from the CD55 family, comprises full length 791Tgp72, CD55 polypeptide, or all or part of the amino acid sequence Fig. 10. The claims are further drawn to a method of treating a patient with cancer by administering the cancer vaccine of claim 1.

10. The specification discloses that 791Tgp72 has an identical amino acid sequence to CD55 (Fig. 10) and fragments and derivatives thereof can be used as cancer vaccines to induce immune responses such as anti-tumour T-cell responses, enhanced IL-2 production, enhanced natural killer activity, etc. (page 12-13). Fragments of 791Tgp72 or CD55 polypeptide are less than full length, capable of inducing an anti-tumour immune response and include all or part of the SUSHI2 domain of CD55, which includes amino acids 97-159 of full length CD55 (page 13). A derivative is defined as a 791Tgp72 or CD55 polypeptide modified by varying the amino acid sequence of the

protein including insertion, addition, deletion, and/or substitution of one or more amino acids, while maintaining an anti-tumour T-cell response (page 13-14). In addition, derivatives may be linked to a coupling partner, effector molecule, label, drug, toxin, etc. (page 14). A therapeutically effective amount is defined as an amount sufficient to show benefit to an individual, wherein the amount, rate and time course of administration will depend on the nature and severity of what is treated (page 20).

11. The instant disclosure fails to meet the enablement requirement for the following reasons:

The specification does not provide any guidance or exemplify that the claimed vaccine induces protective immunity against any cancer. The specification indicates that the vaccine stimulates an anti-tumour T-cell response, but does not give any definitive evidence that the response is able to **protect** a patient from developing cancer. The fact that an agent is able to stimulate an anti-tumour T-cell response does not necessarily mean that it is capable of generating the immunoprotective response needed to fulfill the definition of a vaccine. Furthermore, there is no guidance or exemplification that the vaccine is able to prevent tumor recurrence and to eliminate residual disease.

12. Articles by Ezzell (J. NIH Res, 1995, 7:46-49) and Spitler (Cancer Biotherapy, 1995, 10:1-3) are cited in order to establish the general state of the art and the level of predictability of vaccines. Ezzell reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (page 48, para 6). In addition, Spitler recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work." Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response" (page 1, para 1).

173. The specification discloses that the vaccine encompasses fragments and derivatives of 791Tgp72 or CD55 polypeptide sequences, which are capable of inducing an anti-tumour T-cell response. There are many fragments and derivatives that may or may not perform the same biological functions and the specification does not give any guidance to which fragments and derivatives will exhibit the biological activities as the claimed. Thus, it would be an undue burden to one of ordinary skill in the art to assay for fragments and derivatives of 791Tgp72 or CD55 polypeptide sequences, which are capable of inducing an anti-tumour T-cell response. One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to any 791Tgp72 or CD55 fragment, which includes all or part of the SUSHI2 domain and any derivative with modifications to the protein sequence and applicant has not enabled all of these types of modifications because it has not been shown that these polypeptides are capable of functioning as that which is being disclosed.

14. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly

involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2). Reasonable correlation must exist between the scope of the claims and enablement as set forth, and it cannot be predicted from the disclosure how to use any and all fragments and derivatives. Therefore, in view of the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Natalie A. Davis, Ph.D.
September 27, 2001

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